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Toxoplasma Gondii a risk factor for Alzheimer's disease infection, in Al-Diwaniyah Governorate, Iraq

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Abstract---The results of the serological examination of 35 patients with Alzheimer's disease showed that 21 of them were infected with Toxoplasma Gondii by 60% for the period from the beginning of February until the end of May 2022, the high odds ratio value (OR = 7.87) showed the role of Toxoplasma infection in causing Alzheimer's disease, and there was no effect of age and gender on infection with Toxoplasma parasite in Alzheimer's patients.

Keywords---Toxoplasma Gondii, risk factor, disease infection.

Introduction

Globally, the number of elderly people in the world is increasing day by day, and it is expected that the number of older people over the age of 60 will reach more than two billion people in 2050, as dementia which is more common in the elderly and affects their quality of life will become more Importance, therefore, Alzheimer's disease is the most common cause of dementia among the elderly and will be a threat to humanity in the future, Alzheimer's disease is a brain disease characterized by loss of cognitive functions and behavioral abilities and impairment of a person's life and daily activities (Karabulutet al., 2020). Although scientists have investigated the causes of Alzheimer's disease for years, its etiology remains unclear. So far, the relationship between various infectious types and Alzheimer's disease has been investigated in several studies. (Bayaniet al., 2019; Al-Gharibawi and Al-Wally, 2021).

Studies that dealt with the spread of toxoplasmosis

Toxoplasma Gondii is one of the primary nerve directing organisms and it remains stable in the form of tissue bags preferably in the brain and muscle (Karabulutet

al., 2020). These theories showed that *Toxoplasma* can affect neurons, glial cells, and astrocytes, it can lead to abnormal synthesis of the neurotransmitter, and it can cause neuroinflammation, it can alter host behavior, for dementia in AIDS and immunocompromised patients (Luft & Remington, 1992). Two forms of *T. Gondii* have been recorded, bradyzoites and sporozoites, it accumulate in large quantities of crystalline storage polysaccharide granules similar to amylopectin in the cytoplasm (Karabulut et al., 2020). Therefore, this parasite may be partially responsible for the production of β -amyloid senile plaques (Lyuet et al., 2021)) Based on these studies, our current study aims to investigate whether there is any relationship between *T. Gondii* and AD.

Working Methods

Study Community

Examination of 35 psychiatric patients (Alzheimer's), their ages ranged between 85-95 years, who live in the elderly home, and who visited Al-Diwaniyah Teaching Hospital for psychiatric and mental illnesses and outpatient clinics for specialized doctors were conducted for the period from the beginning of February until the end of May 2022, clinical diagnoses were recorded according to the pre-prepared Diagnostic and Epidemiological Manual. The control group also included 50 healthy people who had no history of mental disorders or other health problems.

Serological Analysis

Blood samples were collected in bottles containing anticoagulants, we find a gel inside it, which helps in separating the serum from red blood cells, blood was drawn from patients and the control using a standard vein sampling, serum was separated from whole blood immediately after blood collection by centrifugation at $3500 \times g$ for 5 min, and stored at -70°C until analysis, specific IgM and anti-*Toxoplasma* IgG antibodies in serum samples were quantitatively measured by mini VIDAS® assays, a compact automated immunoassay system based on the principles of fluorescent enzyme-linked assay (ELFA). The results of antitoxoplasma IgM were automatically confirmed by comparing the signal collected from the sample to a cut-off value confirmed by the device software. For anti-toxoplasma IgG, the signal intensity was measured and the results were directly determined. The ratio of the IgM assay, as IU/ml to the IgG assay was.

Statistical Analysis

Normative tests were performed on quantitative variables before analyzing the data, we used multivariate logistic regression models to estimate the association between *T. Gondii* infection and mental disorders by adjusted odds ratios (ODs) (OR) with a 95% confidence interval (CI) after adjusting for the effect induced by potential influence factors, Such as age and gender among others. All tests were divided and $P < 0.05$ was considered statistically significant. Data management and analysis were performed using SPSS software (version 24.0; SPSS).

Results and Discussion

The results of the serological examination of 35 patients suffering from Alzheimer's disease showed that 21 of them had contracted *Toxoplasma gondii* infection, with an infection rate of 60%. The results of the statistical analysis also showed the role of *Toxoplasma gondii* in causing Alzheimer's disease, where the value of the odds ratio was high (OR = 7.87) compared to the control. Flegr & Horacek (2020) indicated that infection with the *T. gondii* parasite, which infects about 33% of the world's population, is associated with an increased risk of many mental health disorders, the disorders associated with toxoplasmosis were autism (OR = 4.78), schizophrenia (OR = 3.33), attention deficit hyperactivity disorder (OR = 2.50), obsessive-compulsive disorder (OR = 1.86), antisocial personality disorder (OR = 1.63), learning disabilities (OR = 1.59), anxiety disorder (OR = 1.48), Toxoplasmosis can play an important role in causing mental health disorders and its association with schizophrenia is the second strongest link after autism.

The study agreed with Carter (2013) in not only the role of the parasite *T. gondii* in schizophrenia and neurological disorders, but also in Alzheimer's disease or Parkinson's disease, cancer, cardiomyopathy and autoimmune disorders, as shown by the parasite's life cycle, the pathogen interacts with about 3,000 host genes or proteins, including genes for multiple sclerosis, Alzheimer's disease, schizophrenia, bipolar disorder, depression, childhood obesity, Parkinson's disease, attention deficit hyperactivity disorder (multiple sclerosis), and autism. Chegeniet al., (2019) indicated that there is no clear relationship between toxoplasmosis and neurodegenerative diseases, such as Alzheimer's, however, the results of some studies showed a higher prevalence of toxoplasmosis in patients with Alzheimer's, compared to those in the control group and no Reports clarifying the relationship between toxoplasmosis and Alzheimer's disease around the world, the researchers tried to determine whether there is a relationship between *T. gondii* infection and Alzheimer's disease, as the results obtained indicated that the odds ratio OR of antitoxoplasmic *gondii*IgG antibody in patients with Alzheimer's disease was 1.53.

Alzheimer's patients infected with *Toxoplasma gondii* parasite by age

Table (1) indicates that there were no significant differences (p.value = 0.707) between the age groups of Alzheimer's disease and infection with the *Toxoplasma* parasite *T.gondii*, where the highest infection rate was recorded in the age group (76-85) years, reaching 60%, followed by the age group (65-75) years with a rate of 50%, then the age group (86-95) years with a rate of 33.33%.

Table 1
Effect of Toxoplasmosis infection in causing Alzheimer's disease by age groups

Age/year	Total number	Number of injured	Percentage
65-75	10	5	50
76-85	10	6	60
86-95	15	10	33.33
Total	35	21	60

Control	50	8	-----
P value = 0.707			
Odds Ratio (OR)=7.87			

The study (Bouscarenet al.) 2018 showed that Alzheimer's patients with Toxoplasmosis aged 65-69 years infected with a rate of 35.4%, and the age group from 70-74 years infected with 24.2% and the group 75-79 with 219, that is 20.9%, followed by the group 80 years and over with a rate of 19.5%, they also found a relatively large number of elderly people with high antibody titers. The study also agreed with (Rashnoet al. (2016) that it did not record any differences between toxoplasmosis patients with Alzheimer's disease and age groups, explained that toxoplasmosis is one of the most important diseases that affect humans and animals approximately one third of the world's population is infected with toxoplasmosis.

The results also agreed with (Nayeriet al.(2020) that it did not record significant differences among those infected with the Toxoplasma parasite and those with mental illnesses (Alzheimer), and he explained that aging is the most important risk factor for Alzheimer's disease, recurrence rates of Alzheimer's disease have been reported at around 15% and 44% in people aged 65-74 and over 80 in industrialized countries. Also, the study (Rashnoet al. (2016) did not record any differences between Alzheimer's patients with toxoplasmosis and age groups, it was clear that toxoplasmosis is one of the most important diseases that affect humans and animals, nearly one third of the world's population is infected with toxoplasmosis, and there was no significant association between Alzheimer's and toxoplasmosis (0.99 = P), however, there was a statistically significant association between the variables of age, gender, place of residence, type of feeding and infection with *T. gondii* in the sample of patients and control groups.

The results of Chegeniet al. (2019) showed that there are differences between age, race or gender groups, in Alzheimer's patients with toxoplasmosis, education record and socioeconomic status are slightly higher compared to the control group. Alzheimer's patients with Toxoplasmosis were in the age group of 65-69 years with a percentage of 35.4%, and the age group of 70-74 years at 24.2%, and the group 75-79 at 20.9%, followed by the group of 80 years and over with a percentage of 19.5%, and they also explained that a large number of elderly the elderly have high antibody titers, as the results of (Bouscarenet al., 2018) showed.

Alzheimer's patients infected with *Toxoplasma gondii* by gender

The results of the study indicated, as in Table (2), that there were no significant differences between the gender of Alzheimer's patients and their infection with the Toxoplasma parasite (p.value=0.21), and that males were more likely to be infected with 70.58% of females and 50%.

Table 2
Rates of Toxoplasmosis infection in Alzheimer's patients by gender

Gender	Total number	Number of injured	percentage
Male	17	12	70.58

Female	18	9	50
Total	35	21	60
P.value=0.21			

Our study agreed with (Rashnoet al., 2016) who indicated that there were no significant differences between the sex of Alzheimer's patients and their infection with *T. gondii*, which is one of the most prevalent neuropathogens and causes various lesions in a wide range of mammals as an intermediate host, including humans, it is estimated that one third of the world's population is infected with *T. gondii*, however, for a long time, there has been considerable interest in examining the potential role of this parasite in the development of psychiatric disorders, such as Alzheimer's disease (AD). The results differed with (Nayeriet al., 2020) that the specific behavioral changes exhibited by the parasite differ according to the gender of the intermediate host, one study showed gender differences in the clinical phenotype and progression of Alzheimer's disease, this suggests that women are more protected than men in the prodromal phases, but later show higher rates of cognitive brain atrophy, the results of an experimental study also showed that the gender of the host plays an important role in determining the altered brain and behavioral changes after infection with *Toxoplasma gondii* in female mice, *T. gondii* infection alters the expression of genes involved in forebrain development, neurogenesis, and sensorimotor coordination, but in male mice, infection modulates genes related to olfactory function (Xiao et al., 2014; Shojaeet al., 2018).

Manipulation of host behavior by the parasite makes infected male rats more attractive to females, also, uninfected females spend more time near infected males and give them more fertility opportunities, thus creating more ways of sexual transmission by the parasite itself, humans infected with the *Toxoplasma* parasite exhibit a variety of abnormal behaviors, from suicide and depression to stuttering, these behaviors are seen as so serious that they constitute a public health problem, it is not clear whether the parasite is a cause or merely a sign of these behaviors, but there is evidence for both, some of these behaviors are linked to changes in steroid hormones, namely estrogen in women and testosterone in men (James & Grech, 2018).

And (Li et al. (2015) indicated that females are more sensitive to Alzheimer's and *Toxoplasma gondii* than males, microRNA-132 (miR-132) has been shown to affect multiple neuronal functions and dysregulation is associated with several neurological disorders, as acute toxoplasmosis infection induces miR-132 expression in vitro and in vivo, mice were infected with *T. gondii* PRU strain and assessed after 5 months in six brain regions (cortex, hypothalamus, cerebellum, olfactory bulb and hippocampus) by qPCR and it was found that acute *T. gondii*-infection increases the expression of miR. 132, chronic injury has the opposite effect, and the effect differed between different regions of the brain in a gender-dependent manner, as females showed more sensitivity than males.

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